CLAIMS

I CLAIM:

1. A method of increasing the potency of an anti-microbial agent comprising co-administering to patient infected with an ABC transporter-mediated multidrug resistant microbe:

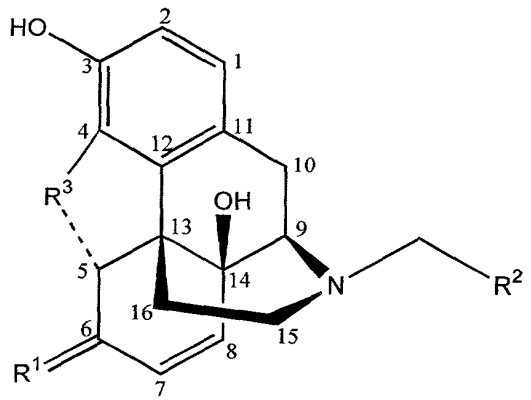
(a) a dose of an anti-microbial agent, wherein the anti-microbial agent is a substrate of an ABC drug transporter; and

(b) a dose of an opioid inhibitor of the ABC drug transporter, wherein the dose of the opioid inhibitor of the ABC drug transporter is sufficient to reduce efflux of the anti-microbial agent from the microbe.

2. The method of claim 1, wherein the ABC drug transporter is a homologue of human PGP1a.

3. The method of claim 1, wherein the anti-microbial agent is selected from the group consisting of the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

4. The method of claim 1, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

5. The method of claim 1, wherein the opioid inhibitor of the ABC drug transporter is selected from the group consisting of naltrexone, naloxone and nalmefene.

6. The method of claim 1, wherein the microbe causing the microbial infection is selected from the group consisting of *Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, LactobacilIus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas, Candida, Plasmodium, Leishmania, Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella, Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium, Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio*, and *Yersinia.*

7. The method of claim 1, wherein the opioid inhibitor of the drug transporter is a compound listed in Table 11.

8. The method of claim 1, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

9. A method of increasing the potency of an anti-microbial agent comprising co-administering to patient infected with an ABC transporter-mediated multidrug resistant microbe:

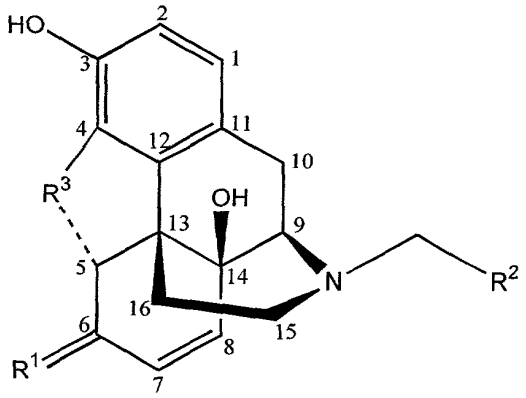
(a) a dose of an anti-microbial agent, wherein the anti-microbial agent is a substrate of an ABC drug transporter; and

(b) a dose of an opioid inhibitor of the ABC drug transporter, wherein the dose of the opioid inhibitor of the ABC drug transporter is sufficient to increase the intracellular concentration of the anti-microbial agent in the microbe.

10. The method of claim 9, wherein the ABC drug transporter is a homologue of human PGP1a.

11. The method of claim 9, wherein the anti-microbial agent is selected from the group consisting of the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

12. The method of claim 9, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH.

13. The method of claim 9, wherein the opioid inhibitor of the ABC drug transporter is selected from the group consisting of naltrexone, naloxone and nalmefene.

14. The method of claim 9, wherein the microbe causing the microbial infection is selected from the group consisting of *Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, LactobacilIus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas, Candida, Plasmodium, Leishmania, Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella, Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium, Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio*, and *Yersinia.*

15. The method of claim 9, wherein the opioid inhibitor of the drug transporter is a compound listed in Table 11.

16. The method of claim 9, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

17. A composition for treating microbial infection comprising:

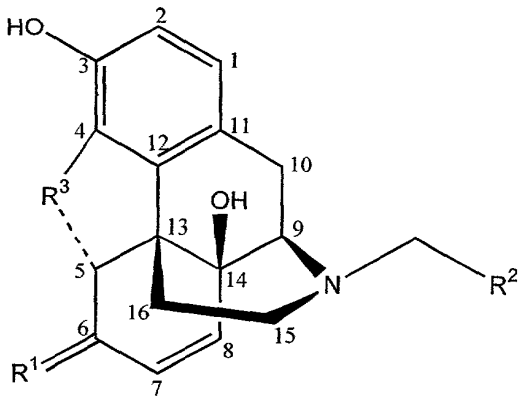
(a) an anti-microbial agent, wherein the anti-microbial agent is a substrate of an ABC drug transporter; and

(b) an opioid inhibitor of the ABC drug transporter.

18. The composition of claim 17, wherein the ABC drug transporter is a homologue of human PGP1a.

19. The composition of claim 17, wherein the anti-microbial agent is selected from the group consisting of the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

20. The composition of claim 17, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

21. The composition of claim 17, wherein the opioid inhibitor of the ABC drug transporter is selected from the group consisting of naltrexone, naloxone and nalmefene.

22. The composition of claim 17, wherein the microbe causing the microbial infection is selected from the group consisting of *Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, LactobacilIus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas, Candida, Plasmodium, Leishmania, Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella,*

Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium, Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio, and *Yersinia.*

23. The composition of claim 17, wherein the opioid inhibitor of the drug transporter is a compound listed in Table 11.

24. The composition of claim 17, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

25. A method of enhancing the anti-microbial activity of an anti-microbial agent against a microbe comprising:

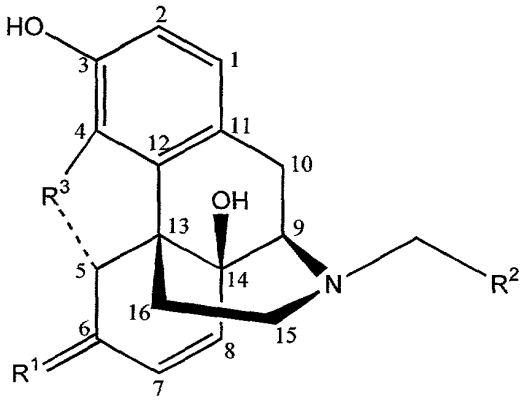
contacting the microbe with the anti-microbial agent and an opioid inhibitor of an ABC drug transporter in an amount effective to inhibit a drug transporter in the microbe, wherein the microbe expresses an ABC drug transporter and the anti-microbial agent is a substrate of the ABC drug transporter.

26. The method of claim 25, wherein the ABC drug transporter is a homologue of human PGP1a.

27. The method of claim 25, wherein the anti-microbial agent is selected from the group consisting of the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the

aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

28. The method of claim 25, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

29. The method of claim 25, wherein the opioid inhibitor of the ABC drug transporter is selected from the group consisting of naltrexone, naloxone and nalmefene.

30. The method of claim 25, wherein the microbe causing the microbial infection is selected from the group consisting of *Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, LactobacilIus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas, Candida, Plasmodium, Leishmania, Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella, Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium, Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio,* and *Yersinia.*

31. The method of claim 25, wherein the opioid inhibitor of the drug transporter is a compound listed in Table 11.

32. The method of claim 25, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

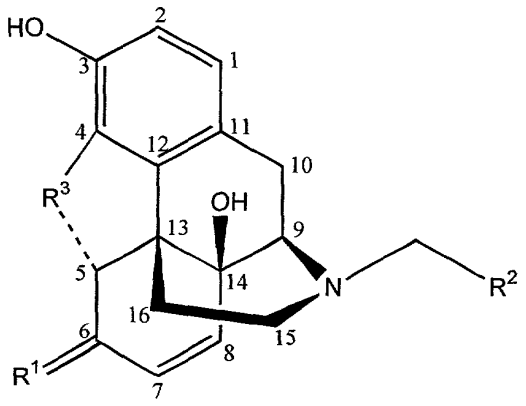
33. A method of suppressing growth of a microbe expressing an ABC drug transporter protein comprising:

contacting the microbe with a sub-therapeutic amount of an anti-microbial agent in the presence of an opioid inhibitor of the ABC drug transporter.

34. The method of claim 33, wherein the ABC drug transporter is a homologue of human PGP1a.

35. The method of claim 33, wherein the anti-microbial agent is selected from the group consisting of the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

36. The method of claim 33, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

37. The method of claim 33, wherein the opioid inhibitor of the ABC drug transporter is selected from the group consisting of naltrexone, naloxone and nalmefene.

38. The method of claim 33, wherein the microbe is selected from the group consisting of *Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, LactobacilIus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas, Candida, Plasmodium, Leishmania, Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella, Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium, Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio*, and *Yersinia.*

39. The method of claim 33, wherein the opioid inhibitor of the drug transporter is a compound listed in Table 11.

40. The method of claim 33, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

41. A method of inhibiting a microbial P-glycoprotein homologue in a patient suffering from a microbial infection comprising administering to the patient a P-glycoprotein inhibiting amount of an inhibitor of an ABC drug transporter, wherein the inhibitor is selected from the group consisting of naltrexone, naloxone and nalmefene,
wherein the inhibitor is administered before, with, or after the administration to the patient of a therapeutic or sub-therapeutic amount of an anti-microbial agent.

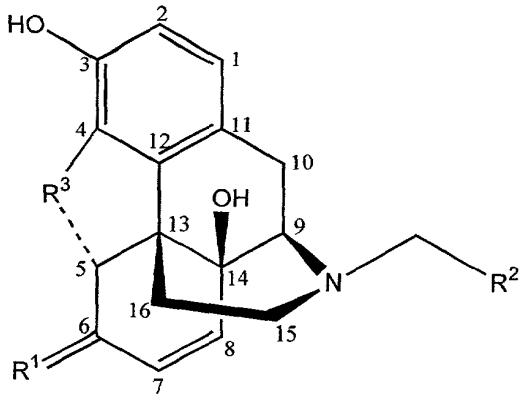
42. The method of claim 41, wherein the ABC drug transporter is a homologue of human PGP1a.

43. The method of claim 41, wherein the anti-microbial agent is selected from the group consisting of the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

44. The method of claim 41, wherein the microbe causing the microbial infection is selected from the group consisting of *Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, LactobacilIus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas, Candida, Plasmodium, Leishmania, Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella, Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium,*

Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio, and *Yersinia.*

45. A method of inhibiting a microbial P-glycoprotein homologue in a patient suffering from a microbial infection comprising administering to the patient a P-glycoprotein inhibiting amount of an inhibitor of an ABC drug transporter, wherein the inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH,

wherein the inhibitor of the ABC drug transporter is administered before, with, or after the administration to the patient of an anti-microbial effective amount of an anti-microbial agent.

46. The method of claim 45, wherein the anti-microbial agent is selected from the group consisting of the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

47. The method of claim 45, wherein the microbe causing the microbial infection is selected from the group consisting of *Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, LactobacilIus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas,*

Candida, Plasmodium, Leishmania, Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella, Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium, Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio, and *Yersinia.*

48. A composition for the treatment of a microbial infection comprising:

(a) an opioid inhibitor of an ABC drug transporter; and

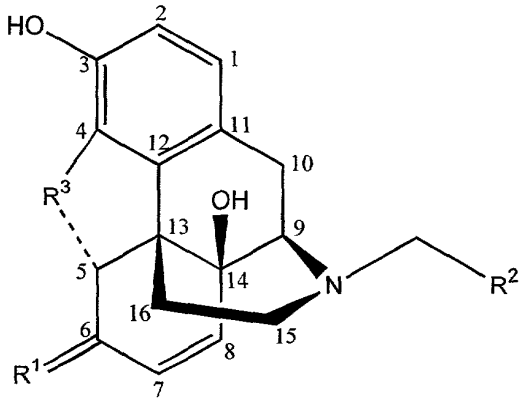
(b) an anti-microbial agent

wherein the opioid inhibitor of the ABC drug transporter is capable of inhibiting a drug transporter protein.

49. The composition of claim 48, wherein the ABC drug transporter is a homologue of human PGP1a.

50. The composition of claim 48, wherein the anti-microbial agent is selected from the group consisting of the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

51. The composition of claim 48, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH.

52. The composition of claim 48, wherein the opioid inhibitor of the ABC drug transporter is selected from the group consisting of naltrexone, naloxone and nalmefene.

53. The composition of claim 48, wherein the microbe causing the microbial infection is selected from the group consisting of *Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, Lactobacillus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas, Candida, Plasmodium, Leishmania, Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella, Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium, Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio*, and *Yersinia.*

54. The composition of claim 48, wherein the opioid inhibitor of the drug transporter is a compound listed in Table 11.

55. The composition of claim 48, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

56. A method of identifying a compound for improved treatment of microbial infections comprising:

(a) identifying an anti-microbial agent;

(b) assaying the ability of the therapeutic agent to be transported across a membrane by an ABC protein; and

(c) repeating the transport assay to determine whether addition of an opioid inhibitor of an ABC drug transporter inhibits transport of the therapeutic agent across the membrane, whereby the compound that is transported by an ABC protein and whose ABC protein-mediated transport is inhibited by the opioid inhibitor of the ABC drug transporter is identified.

57. Method of enhancing the potency of an anti-microbial agent identified by the method of claim 56 comprising:

co-administering a therapeutic amount of the compound and an amount of an opioid inhibitor of an ABC drug transporter capable of inhibiting a drug transporter, wherein the amount of the opioid inhibitor of the ABC drug transporter is sufficient to reduce transport of the compound across a biological membrane.

58. A method for screening for an opioid inhibitor of an ABC drug transporter, comprising determining whether a potential opioid inhibitor inhibits growth of a microbial cell in the presence of sub-therapeutic amount of anti-microbial agent,

wherein the microbial cell expresses an ABC drug transporter, and

wherein said determining comprises comparing the growth of the microbial cell which expresses the ABC drug transporter, with growth of a second microbial cell which

does not produce the ABC drug transporter, wherein the first and second microbial cells are grown in the presence of the sub-therapeutic amount of the anti-microbial agent.

59. A method for screening for an opioid inhibitor of an ABC drug transporter, comprising:

contacting a potential opioid inhibitor of an ABC drug transporter protein with the ABC drug transporter protein in the presence of a compound selected from the group consisting of naltrexone, naloxone and nalmefene, wherein the compound is detectably labeled;

measuring the amount of detectably labeled compound bound to the ABC drug transporter; and

comparing the measured amount to the amount of detectably labeled compound bound by the ABC drug transporter when the drug transporter is contacted with the compound alone,

whereby a measured amount lower than the amount of compound bound to the ABC drug transporter when contacted alone identifies an opioid inhibitor of the ABC drug transporter.

60. The method of claim 59, wherein the potential opioid inhibitor of the ABC drug transporter is selected from the compounds listed in Table 11.

61. A method of treating a microbial infection in an animal, comprising administering to the animal suffering from the infection an anti-microbial agent and an ABC drug transporter inhibitor in an amount sufficient to increase the intracellular concentration of the anti-microbial agent in the microbe,

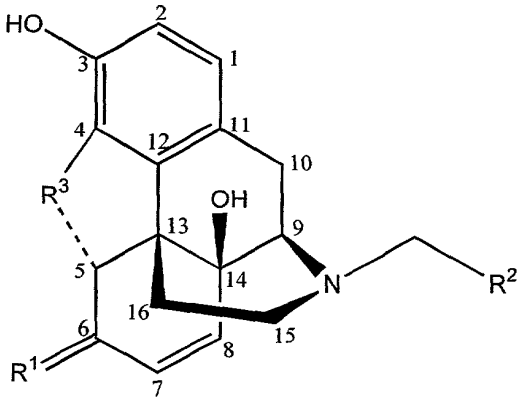
wherein the ABC drug transporter inhibitor increases the susceptibility of the microbe to the anti-microbial agent, and

wherein the ABC drug transporter inhibitor is selected from the group consisting of naltrexone, naloxone and nalmefene.

62. A method of treating a microbial infection in an animal, comprising administering to the animal suffering from the infection an anti-microbial agent and an ABC drug transporter inhibitor in an amount sufficient to increase the intracellular concentration of the anti-microbial agent in the microbe,

wherein the ABC drug transporter inhibitor increases the susceptibility of the microbe to the anti-microbial agent, and

wherein the ABC drug transporter inhibitor is a compound of the formula:



wherein R^1 is CH_2 or O;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH.